APPENDIX B

PENDING CLAIMS

1. (As filed) A method of treating a neoplasia in a mammal, said method comprising administering to said mammal a serum-stable nucleic acid-lipid particle comprising a nucleic acid portion that is fully encapsulated within the lipid portion, wherein said administration is by injection at an injection site that is distal to said neoplasia in said mammal.

2. (As filed) A method of treating a neoplasia in a mammal in accordance with claim 1, wherein said nucleic acid comprises an expressible gene.

3. (As filed) A method of treating a neoplasia in a mammal in accordance with claim 2, wherein said expressible gene encodes a member selected from the group consisting of therapeutic polypeptides and therapeutic polynucleotides.

4. (Once amended) A method of treating a neoplasia in a mammal in accordance with claim 2, wherein said gene is heterologous.

5. (As filed) A method of treating a neoplasia in a mammal in accordance with claim 3, wherein said gene is a member selected from the group consisting of genes encoding suicide enzymes, toxins and ribozymes.

6. (Once amended) A method of treating a neoplasia in a mammal in accordance with claim 2, wherein said gene encodes a member selected from the group consisting of herpes simplex virus thymidine kinase (HSV-TK), cytosine deaminase, xanthine-guaninephosphoribosyl transferase, purine nucleoside phosphorylase, cytochrome P450 2B1.

7. (As filed) A method of treating a neoplasia in a mammal in accordance with claim 2, wherein said gene is homologous.

8. (As filed) A method of treating a neoplasia in a mammal in accordance with claim 2, wherein said gene encodes a member selected from the group consisting of proto-oncogenes, cytokines, immune stimulatory proteins and anti-angiogenic proteins.

9. (As filed) A method of treating a neoplasia in a mammal in accordance with claim 2, wherein said gene is a member selected from the group consisting of IL-2, IL-12, IL-15 and GM-CSF.

10. (As filed) A method of treating a neoplasia in a mammal in accordance with claim 2, wherein a therapeutically effective amount of said gene is generated at said neoplasia.

11. (As filed) A method of treating a neoplasia in a mammal in accordance with claim 1, wherein said nucleic acid-lipid particle comprises a protonatable lipid having a pKa in the range of about 4 to about 11.

12. (As filed) A method of treating a neoplasia in a mammal in accordance with claim 11, wherein said protonatable lipid is a member selected from the group consisting of DODAC, DODAP, DODMA, DOTAP, DOTMA, DC-Chol, DMRIE, DSDAC and mixtures thereof.

13. (As filed) A method of treating a neoplasia in a mammal in accordance with claim 1, wherein said nucleic acid-lipid particle comprises a lipid conjugate that prevents aggregation during formulation.

14. (As filed) A method of treating a neoplasia in a mammal in accordance with claim 13, wherein said lipid conjugate is a member selected from the group consisting of PEG-lipids and PAO-lipids.

15. (As filed) A method of treating a neoplasia in a mammal in accordance with claim 13, wherein said lipid conjugate is reversibly associated with an outer lipid monolayer, and wherein said lipid conjugate exchanges out of said outer lipid monolayer at a rate faster than PEG-CerC20.

16. (As filed) A method of treating a neoplasia in a mammal in accordance with claim 1, wherein said nucleic acid-lipid particle is substantially devoid of detergents and organic solvents.

17. (As filed) A method of treating a neoplasia in a mammal in accordance with claim 1, wherein a therapeutically effective amount of said nucleic acid-lipid particle accumulates at said neoplasia.

18. (As filed) A method of treating a neoplasia in a mammal in accordance with claim 1, wherein a therapeutic effect is detected at the site of said neoplasia.

19. (As filed) A method of treating a neoplasia in a mammal in accordance with claim 17, wherein said therapeutically effective amount comprises greater than about 0.5% of an administered dose.

20. (As filed) A method of treating a neoplasia in a mammal in accordance with claim 1, wherein said nucleic acid-lipid particle has a diameter of about 50 nm to about 200 nm.

21. (As filed) A method of treating a neoplasia in a mammal in accordance with claim 20, wherein said nucleic acid-lipid particle has a diameter of about 60 nm to about 130 nm.

22. (As filed) A method of treating a neoplasia in a mammal in accordance with claim 20, wherein said nucleic acid-lipid particles are of a uniform size.

23. (As filed) A method of treating a neoplasia in a mammal in accordance with claim 1, wherein said nucleic acid-lipid particle has a nucleic acid to lipid ratio of greater than about 3 mg nucleic acid to mmole of lipid.

24. (As filed) A method of treating a neoplasia in a mammal in accordance with claim 23, wherein said particle has a nucleic acid to lipid ratio of greater than about 14 mg nucleic acid to mmole of lipid.

25. (As filed) A method of treating a neoplasia in a mammal in accordance with claim 23, wherein said particle has a nucleic acid to lipid ratio of greater than about 25 mg nucleic acid to mmole of lipid.

26. (As filed) A method of treating a neoplasia in a mammal in accordance with claim 1, wherein said nucleic acid remains at least 90% intact when said particle containing about 1 μg DNA is treated with about 100 U DNAse 1 in digestion buffer at 37°C for 30 min.

28. (As filed) A method of treating a neoplasia in a mammal in accordance with claim 1, wherein said administering is performed at least once per eight weeks.

35. (New) A method of treating a neoplasia in a mammal, in accordance with claim 5, wherein said gene encodes a suicide enzyme.

36. (New) A method of treating neoplasia in a mammal in accordance with claim 35, further comprising administering a prodrug.

37. (New) A method of treating a neoplasia in a mammal in accordance with claim 36, wherein said prodrug is administered after the serum-stable nucleic acid-lipid particle.

38. (New) A method of treating a neoplasia in a mammal in accordance with claim 36, wherein said prodrug is administered before the serum-stable nucleic acid-lipid particle.

39. (New) A method of treating a neoplasia in a mammal in accordance with claim 9, further comprising administering a chemotherapeutic agent.

40. (New) A method of treating a neoplasia in a mammal in accordance with claim 39, wherein the chemotherapeutic agent is administered after the serum-stable nucleic acid-lipid particle.

41. (New) A method of treating a neoplasia in a mammal in accordance with claim 39, wherein the chemotherapeutic agent is administered before the serum-stable nucleic acid-lipid particle.

42. (New) A method of treating a neoplasia in a mammal in accordance with claim 1, wherein the lipid portion comprises a cationic lipid and a neutral lipid.

43. (New) A method of treating a neoplasia in a mammal in accordance with claim 42, wherein the cationic lipid is DODAC.

44. (New) A method of treating a neoplasia in a mammal in accordance with claim 42, wherein the neutral lipid is DOPE.

45. (New) A method of treating a neoplasia in a mammal in accordance with claim 42, wherein the lipid portion further comprises a PEG-lipid.

46. (New) A method of treating a neoplasia in a mammal in accordance with claim 42, wherein the lipid portion further comprises cholesterol.

47. (New) A method of treating a neoplasia in a mammal, said method comprising administering to said mammal a serum-stable nucleic acid-lipid particle comprising a nucleic acid portion that is fully encapsulated within the lipid portion,

wherein said administration is by injection at an injection site that is distal to said neoplasia in said mammal; and

wherein said neoplasia is responsive to the gene product of the nucleic acid.

48. (New) A method of treating a neoplasia in a mammal, said method comprising administering to said mammal a serum-stable nucleic acid-lipid particle comprising a nucleic acid portion that is fully encapsulated within the lipid portion,

wherein said administration is by injection at an injection site that is distal to said neoplasia in said mammal; and

wherein cells of said neoplasia are transfectable by said nucleic acid-lipid particle.

49. (New) The method of claim 47, wherein said nucleic acid encodes a member selected from the group consisting of: suicide enzymes, toxins, tumor suppressor genes, and cytokines.

50. (New) The method of claim 47, wherein said nucleic acid encodes a suicide enzyme.

51. (New) The method of claim 47, wherein said nucleic acid encodes a toxin.

52. (New) The method of claim 47, wherein said nucleic acid encodes a tumor suppressor protein.

53. (New) The method of claim 47, wherein said nucleic acid encodes a cytokine.

54. (New) The method of claim 50, wherein the suicide enzyme is a member selected from the group consisting of: HSV-TK, purine nucleoside phosphorylase, and cytosine deaminase.

55. (New) The method of claim 50, wherein the neoplasia is melanoma.

56. (New) The method of claim 50, wherein the neoplasia is colorectal cancer.

57. (New) The method of claim 50, wherein the neoplasia is sarcoma.

58. (New) The method of claim 51, wherein the toxin is *Pseudomonas* exotoxin.

59. (New) The method of claim 51, wherein the tumor suppressor protein is apoptin.

60. (New) The method of claim 51, wherein the cytokine is IL-12.

61. (New) The method of claim 51, wherein administration of the serum-stable nucleic acid-lipid particle is intravenous.